

The Chernobyl Disaster: Cancer following the Accident at the Chernobyl Nuclear Power Plant

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Received for publication March 20, 2005; accepted for publication March 30, 2005.

THE ACCIDENT

The Chernobyl nuclear power plant, located in Ukraine about 130 km north of the capital of Kiev and about 10 km south of the border with Belarus, was the scene of the most severe accident that has ever occurred in the nuclear industry. On April 26, 1986, two violent explosions destroyed the core of unit 4 of the power plant and the roof of the building, resulting in a series of fires and in massive releases of radioactive materials into the atmosphere. The releases consisted of gases, aerosols, and finely fragmented nuclear fuel particles. From the radiologic point of view, iodine-131 (¹³¹I) and cesium-137 (¹³⁷Cs) are the most important radio-nuclides to consider (1, 2). During the 10 days of massive releases, the wind direction changed frequently, so that all areas surrounding the reactor received some fallout at one time or another. In addition, rainfall occurred in an irregular pattern, causing varying degrees of deposition. The releases of radioactive materials were such that contamination of the ground was found to some extent in every country in the Northern Hemisphere (3). However, the most contaminated areas were in Belarus, Russia, and Ukraine (table 1).

Several categories of people were affected by the accident: 1) workers, who can be divided into two groups: a) the approximately 600 persons involved in emergency measures during the first day of the accident (the so-called emergency workers), and b) the hundreds of thousands of people who, from 1986 to 1989, were sent in to the power station or the zone surrounding it for decontamination work, sarcophagus construction, and other cleanup operations; this second group of workers is usually referred to as cleanup workers or liquidators; and 2) members of the general public, including a) the evacuees, mainly from the area within 30 km of the damaged reactor; about 100,000 persons were evacuated within 2 weeks of the accident and 16,000 more before the autumn of 1986, for a total of 116,000

persons, and b) the approximately 5 million residents of the contaminated areas in Belarus, Ukraine, and Russia (2).

EMERGENCY WORKERS

Dosimetry

The most important exposures for emergency workers were due to external irradiation. Because all of the dosimeters worn by the workers were overexposed, they could not be used to estimate doses. Estimates were obtained by means of biologic dosimetry for the treated workers.

Short-term health effects

A number of the emergency workers, who dealt with the fires and other emergency situations within hours of the accident, developed radiation sickness, that is, health effects due to massive cell damage and cell death, regarded as a deterministic event. A total of 134 workers were treated clinically for radiation sickness (2). Of these, all had bone marrow symptoms and some demonstrated symptoms related to other organs such as the intestines, lung, and eye.

The clinical treatment was generally successful for those who received whole-body doses of less than 4 Gy and was moderately successful for those who received doses of 4–6 Gy, but the fatality rate for doses above 6 Gy was very high. Twenty-two workers received whole-body doses of external irradiation in excess of 4 Gy and 21 workers doses in excess of 6 Gy, with fatality rates of 32 percent and 95 percent, respectively (2). The experience gained in terms of clinical treatment of so many persons with severe radiation sickness should provide valuable information in the event of future nuclear incidents.

TABLE 1. Contaminated areas* of European countries following the 1986 Chernobyl nuclear power plant accident†

Country	Size of contaminated area (km ²)	
	37–185 kBq/m ²	>185 kBq/m ²
Russia	49,800	8,100
Belarus	29,900	16,600
Ukraine	37,200	5,700
Sweden	12,000	
Finland	11,500	
Austria	8,600	
Norway	5,200	
Bulgaria	4,800	
Switzerland	1,300	
Greece	1,200	
Slovenia	300	
Italy	300	
Moldova	80	

* Defined as those in which the ¹³⁷Cs deposition density resulting from the Chernobyl accident was >37 kBq/m².

† Adapted from Izrael et al. (90).

CLEANUP WORKERS

Dosimetry

The cleanup workers, sent to the Chernobyl power plant from 1986 through 1989 to mitigate the consequences of the accident, received radiation exposures primarily due to external irradiation from gamma-emitting radionuclides. The highest doses were received by the cleanup workers, mostly males aged 20–45 years, who were employed in 1986–1987 in the 30-km exclusion zone. Lower doses were received by the remainder of the cleanup workers who came to the reactor site in 1988–1989 (a small number of workers are still involved).

External doses from gamma radiation. Doses from external irradiation have been recorded, to the extent feasible, in national registries. The national registry data for Belarus, Russia, and Ukraine, presented in table 2, show that the number of cleanup workers and the average of the doses recorded decreased from year to year, with mean doses of about 0.14 Gy in 1986, 0.09 Gy in 1987, and 0.04 Gy in 1988–1989, in accordance with a decrease in the annual dose limits for most cleanup workers, from 0.25 Gy in 1986, to 0.1 Gy in 1987, and to 0.05 Gy from 1988 onward.

Within the framework of epidemiologic studies conducted by the National Cancer Institute and the International Agency for Research on Cancer, efforts have been made to develop a time-and-motion method of dose assessment that would be applicable to all subjects (4). Gamma radiation levels were measured at various points at the reactor site, and the dose to the worker was estimated as a function of the location of work and of time spent there. The results will be validated by using biodosimetry.

Internal doses. Because of the abundance of ¹³¹I and of shorter-lived radioiodines in the environment of the reactor during the accident, the cleanup workers on site during the first few weeks after the accident may also have received substantial thyroid doses from internal irradiation, since the thyroid gland concentrates radioiodines. Information on the thyroid doses is very limited and imprecise, however. Tentative thyroid dose estimates, based on direct thyroid measurements of 600 cleanup workers, showed the following distribution (5): 64.0 percent of workers were exposed to less than 0.15 Gy, 32.9 percent to 0.15–0.74 Gy, 2.6 percent to 0.75–1.4 Gy, and the remaining 0.5 percent to 1.5–3.0 Gy. The average thyroid dose estimate is about 0.21 Gy.

Cancer

The several hundred thousand cleanup workers, drawn mainly from Belarus, Ukraine, and the Russian Federation, did not experience radiation sickness unless they were among the emergency workers described above. For the rest of the Chernobyl workers, the dose was protracted over days, weeks, or even months. Thus, the health outcomes of greatest concern are the long-term stochastic effects such as cancer induction.

All cleanup workers were eligible to be enrolled in Chernobyl state registries and received free annual medical examinations. Although not all cleanup workers were registered, the state registries have been the basis for nearly all epidemiology studies that have assessed long-term health effects. However, the “official doses” contained in the state registries are missing for many (refer to table 2) and are of uncertain accuracy and precision for others. Secondly, diagnostic information in the registries may be of questionable quality and requires further independent confirmation. Finally, comparisons with external population rates may be misleading because the cleanup workers who attend the medical examinations will all generally be screened much more frequently than the general population. These limitations should be borne in mind in interpreting epidemiologic studies that depend on registry data.

Studies to date have focused on the occurrence of leukemia and thyroid cancer, given their short minimal latency period and sensitivity to radiation. In addition, a few studies of the occurrence of other cancers have been reported (6, 7).

Leukemia

An early cohort study of Estonian cleanup workers reported no cases of leukemia occurring among 4,742 men between 1986 and 1993 (7). However, this study was limited by small numbers and a relatively short follow-up.

A much larger cohort study among 168,000 Russian liquidators was reported by Ivanov et al. (8). On the basis of 48 cases of leukemia through 1993 (including chronic lymphocytic leukemia, generally believed not to be radio-sensitive), they found a statistically significant standardized incidence ratio of 1.77 (95 percent confidence interval: 1.22, 2.47) compared with the Russian population for the period 1990–1995. Before 1990, the standardized incidence ratio was much lower and was not significant. A statistically

TABLE 2. Distribution of doses from external radiation to cleanup workers, as recorded in national registries, following the 1986 Chernobyl nuclear power plant accident*

Country and time period	No. of cleanup workers	Percentage for whom dose is known	External dose (mGy)			
			Mean	Median	75th percentile	95th percentile
Belarus						
1986	68,000	8	60	53	93	138
1987	17,000	12	28	19	29	54
1988	4,000	20	20	11	31	93
1989	2,000	16	20	15	30	42
1986–1989	91,000	9	46	25	70	125
Russian Federation						
1986	69,000	51	169	194	220	250
1987	53,000	71	92	92	100	208
1988	20,500	83	34	26	45	94
1989	6,000	73	32	30	48	52
1986–1989	148,500	63	107	92	180	240
Ukraine						
1986	98,000	41	185	190	237	326
1987	43,000	72	112	105	142	236
1988	18,000	79	47	33	50	134
1989	11,000	86	35	28	42	107
1986–1989	170,000	56	126	112	192	293

* Data are from Cardis et al. (91), Kenigsberg and Kruk (92), and the Ministry of Health of Ukraine (93).

significant excess relative risk of 4.3 per Gy (95 percent confidence interval: 0.83, 7.75) was observed in the cohort. This estimate appeared comparable in magnitude to the leukemia risk estimate for the survivors of atomic bombings who were older than 20 years of age at the time of the bombings (excess relative risk = 3.70 per Gy, averaged over sexes (2)).

In a further study of Russian cleanup workers, Ivanov et al. (9) studied the occurrence of leukemia in a cohort of 71,870 workers engaged in recovery operations within the 30-km zone between 1986 and 1990 and for whom individual external radiation dose estimates were available in the Russian National Medical and Dosimetric Registry. They observed 58 cases of pathologically confirmed leukemia between 1986 and 1998. After excluding chronic lymphocytic leukemia ($n = 16$), they obtained a standardized incidence ratio of 2.5 (90 percent confidence interval: 1.3, 3.7) comparing those who received doses of 150–300 mGy to those whose doses were below 150 mGy and estimated an excess relative risk at 1 Gy of 6.7 (90 percent confidence interval: 0.8, 23.5).

Buzunov et al. (10) studied leukemia occurrence among approximately 175,000 cleanup workers in Ukraine. They compared the rates of leukemia for those first employed in 1986 with those for workers employed in 1987, when doses were lower; they found that the rate of leukemia had approximately doubled among those who first worked in

1986. However, there was no obvious time trend among those employed in 1986.

To date, the results of one analytic study—a case-control study nested within a cohort of cleanup workers—have been reported (11). A total of 36 nonchronic lymphocytic leukemia cases diagnosed between 1986 and 1993 were compared with controls (case:control ratio of 1:3). The mean dose for cases was lower than that for the corresponding controls; nevertheless, an elevated, nonstatistically significant relative risk was observed with the highest exposures.

Thyroid cancer

In the study of 4,742 Estonian cleanup workers referred to above, Inskip et al. (12) did not find an excess of thyroid cancer 9 years after the accident, and subsequent extended follow-up of this cohort did not show any increase in the risk of thyroid cancer up to 16 years after the accident. In an early study of Russian cleanup workers, Ivanov et al. (8, 13) did find a suggestion of increased risk of thyroid cancer for early workers, that is, those on site within several weeks of the accident who had been exposed to radioactive iodines in addition to the external radiation to which all workers were exposed.

A later follow-up study of Russian cleanup workers by Ivanov et al. (14) reported on thyroid cancer incidence among 99,024 workers. A total of 58 thyroid cancers were

detected between 1986 and 1998, which yielded a standardized incidence ratio of 4.33 (95 percent confidence interval: 3.29, 5.60) compared with Russian population rates for men. There was no significant association with risk of thyroid cancer when considering internal comparisons within the cohort based on external dose, but the authors ascribed this to lack of data on internal doses and the possibility of increased detection because of the regular medical examinations.

Other cancers

In general, there are very few data related to other individual cancer risks among cleanup workers. There have been reports, however, of an increase in all solid cancers combined occurring among Russian cleanup workers (15, 16). In a cohort of approximately 56,000 such workers, who received doses of up to 300 mGy, 1,370 cancers were observed between 1991 and 2001 (16). There was a suggestion of an association with radiation dose that was not significant either in an internal analysis or in comparison with Russian population rates. Similar results were obtained in a much smaller cohort of Russian cleanup workers (15).

Summary

Because cleanup workers largely receive higher doses than the general population, studies of such workers potentially have greater statistical power to measure effects. The use of official doses from the registries is problematic, as mentioned above. For this reason, case-control studies conducted within registry-based cohorts offer the best chance for estimating doses by means of reconstruction techniques and also offer the potential for determining possible confounders or effect modifiers.

To date, the available data support a measurable increase in risk of leukemia among cleanup workers; the evidence with regard to thyroid cancer is more equivocal, which may be due to the difficulty in estimating internal doses to the thyroid among the early emergency workers who potentially are at the greatest risk. For other solid cancers, little can be said, presumably because of a longer minimal latency period and lower risks per dose. It is hoped that future studies of cleanup workers will clarify information in all these areas.

RESIDENTS OF CONTAMINATED AREAS

Dosimetry

The most important pathways of exposure for the residents of contaminated regions were found to be external exposure from radionuclides deposited on the ground and internal exposure resulting from ingesting milk and other foodstuffs contaminated with ^{131}I , ^{134}Cs , and ^{137}Cs . In the first few months, because of the significant release of the short-lived ^{131}I , the thyroid was the most exposed organ. The main route of internal exposure for thyroid dose was the pasture-cow-milk pathway, with a secondary component from inhalation. After a few months, when ^{131}I had decayed away, the most important contributors to the doses to all organs and tissues were ^{137}Cs and, to a lesser degree, ^{134}Cs .

TABLE 3. Distribution of the Ukrainian and Belarusian cohort subjects according to the geometric mean of their thyroid doses following the 1986 Chernobyl nuclear power plant accident*

Thyroid dose interval (Gy)	Relative percentage of subjects	
	Ukraine	Belarus
0–0.3	57	43
0.31–1	26	29
>1	17	28
All	100	100

* Adapted from Likhtarev et al. (20).

Thyroid doses. The assessment of thyroid doses is based on measurements of external gamma radiation performed by means of radiation detectors placed against the neck. Within a few weeks following the accident, approximately 350,000 of these measurements were made in Belarus, Ukraine, and Russia (17–19). The thyroid dose estimates obtained in this manner for the approximately 25,000 subjects of two epidemiologic cohort studies conducted in Belarus and in Ukraine are presented in table 3 (20); the distribution of the thyroid doses is similar in the two countries, with medians of about 0.3 Gy and a substantial fraction of doses exceeding 1 Gy.

For the persons whose exposure was not measured but who lived in areas where many persons had been measured, the thyroid doses are reconstructed on the basis of the statistical distribution of the thyroid doses estimated for the people for whom measurements are available, together with knowledge of the dietary habits of the persons considered. Finally, the thyroid doses for people who lived in areas with very few or no direct thyroid measurements within a few weeks after the accident are reconstructed by means of associations using available data on ^{131}I or ^{137}Cs deposition, exposure rates, or concentrations of ^{131}I in milk (2). Catalogues of thyroid dose estimates are available for the exposed populations of Belarus, Russia, and Ukraine (18, 21, 22).

Bone marrow doses. Bone marrow doses also have been estimated for the approximately 5 million residents of the contaminated areas who were not evacuated. Following the first few weeks of the accident, when ^{131}I was the main contributor, doses relatively homogeneous over all organs and tissues of the body were delivered at much lower rates by ^{137}Cs and ^{134}Cs , so the bone marrow doses are generally assumed to be equal to the whole-body doses. The average bone marrow doses from ^{134}Cs and ^{137}Cs that the residents of contaminated areas received during the first 10 years after the accident are estimated to be about 0.01 Gy (table 4).

Thyroid cancer

As described earlier, the principal component of the massive releases of radioactive materials into the environment from the Chernobyl accident was ^{131}I , which is primarily absorbed by the thyroid gland. Because of the small

TABLE 4. Summary of estimated average bone marrow doses (excluding thyroid doses) to populations of areas contaminated by the Chernobyl nuclear power plant accident (1986–1995)*

Country	Estimated arithmetic mean bone marrow dose (mGy)		Total
	External exposure	Internal exposure	
Belarus	5	3	8
Russian Federation	4	2.5	6.5
Ukraine	5	6	11

* Information in this table was based on Bennett et al. (94).

size of the gland in children and their high intake of milk, much of which was contaminated, children generally received the highest thyroid doses (3, 17).

Thyroid cancer among those exposed in childhood. The thyroid gland in children is especially radiosensitive, and childhood exposure to relatively low doses of external radiation (approximately 0.1 Gy) is known to significantly increase the risk of thyroid tumors (2, 23–25). Thus, one of the main health concerns related to the Chernobyl disaster was the risk of developing radiation-related thyroid diseases, particularly neoplasms. Five years after the accident, the first report of an unusually high occurrence of childhood thyroid cancer in the contaminated regions of Ukraine was published (26). Shortly afterward, a high incidence of thyroid cancer in children also was observed in Belarus (27–30) and later in the contaminated area of Russia (31, 32). Between 1990 and 1998, it has been estimated that close to 2,000 thyroid cancers were diagnosed in the contaminated regions of the three countries (Belarus, Ukraine, and the Russian Federation) among persons less than 18 years of age (2). In Belarus, the enormous rise in pediatric thyroid cancers was especially notable. Compared with the usual incidence rate of about 1 case per million children per year, the rate in Belarus was nearly 30 times higher less than 10 years after the accident (33). Between 1992 and 2000, about 4,000 thyroid cancers were diagnosed in the contaminated regions of Belarus, Russia, and Ukraine (34).

Early on, it was thought that better reporting and screening might be partly responsible for the large number of thyroid cancers diagnosed so soon after the accident (35–37). However, more recent epidemiologic data have demonstrated that the enhanced risk is associated with the radioiodine exposure (38–50).

While it is now unquestionable that radiation exposure from the Chernobyl accident has resulted in a substantially elevated incidence of thyroid cancer among persons exposed at young ages, most studies to date have been descriptive and few have quantified risks or have evaluated factors that may modify risk. Several ecologic studies have been conducted in the three countries most affected (39–42, 51). On the basis of collective dose, Jacob et al. (41) reported a linear dose response for the three countries and an excess absolute risk per 10,000 person-year-Gy of 2.3

(95 percent confidence interval: 1.4, 3.8). In a later study (51), performed in Belarus and the Bryansk region of Russia, results were very similar. The excess absolute risk per 10,000 person-year-Gy was 2.1 (95 percent confidence interval: 1.0, 4.5), and the excess relative risk per Gy was 23 (95 percent confidence interval: 8.6, 82). The risk was statistically significantly elevated even in the lowest dose group, which received an average of only 0.05 Gy.

The first population-based case-control study of thyroid cancer and radiation from Chernobyl, comprising 107 young thyroid cancer cases and double the number of controls, was conducted in Belarus (38). This study was unique because it tried to account for possible ascertainment bias by choosing one general control group and another control group comprising persons who had an opportunity to be diagnosed with thyroid cancer similar to that of the cases. Doses were calculated based on the mean doses estimated for adults living in the same villages or towns, taking into account the study subjects' age and location at the time of the accident. A strong association between thyroid cancer and estimated dose was observed. When exposures of less than 0.3 Gy were compared with those equal to or greater than 0.3 Gy, the odds ratios for the latter ranged from 2.1 to 8.3 depending on which subgroups of controls were used as the comparison population. A small population-based case-control study of 26 cases and 52 controls, all under the age of 19 years at the time of the accident, has recently been completed in Russia. It demonstrated a strong dose response (one-sided $p < 0.01$) (48).

As has been clearly shown for external radiation (2, 23–25), the risk of developing thyroid cancer related to Chernobyl exposure appears to increase with decreasing age at exposure (33, 42–45, 52–54). Comparing the number of thyroid cancer cases reported in Belarus and three oblasts (territorial subdivisions) in Russia with cases in the United Kingdom, Cardis et al. (55) estimated that the risk for children less than 1 year of age at the time of the accident was about five times larger than for those aged 5 years at exposure, and about 40 times greater than for children aged 10 years at exposure. Other studies have also reported greater risks for younger children compared with older children, but the magnitude of the difference was considerably smaller (45). In a new evaluation of time trends in the exposed regions in Ukraine, the absolute risk for developing radiation-related thyroid cancer was similar for children up to age 15 years at the time of the accident (56).

Information is lacking about thyroid cancer risks associated with in utero exposure. Since, in early childhood, the thyroid is very sensitive to radiation, the fetus might also be expected to be extremely vulnerable. However, almost 20 years after the accident, there is little evidence to support the notion that in utero exposure is particularly dangerous to the thyroid. On the basis of the finding of only two thyroid cancers diagnosed before 1999 among persons exposed in utero, it has been postulated that the thyroid gland of the fetus is protected by the mother's physiology (57). Furthermore, the two cases were born a few weeks after the accident, when they would have received some environmental contamination postnatally. Fetal thyroid risk from ^{131}I has also been examined in 400 subjects from the Utah fallout study who were exposed in utero (58); no thyroid

cancers were found, but benign thyroid disease was observed. However, before drawing firm conclusions about the sensitivity of the fetal thyroid, it should be noted that the power to observe excess risks in persons exposed in utero is very limited compared with those exposed as children (aged 1–18 years).

Thyroid cancer among those exposed as adults. There have been few investigations of radiation-related thyroid cancer among adults living in the exposed areas (52). Early on, reports suggested an association between thyroid cancer and adult exposure in Ukraine (26) and in Russia (13). A recent dose-response analysis of thyroid cancer in persons exposed in Bryansk between ages 15 and 69 years found no association with dose (59). On the basis of the current data, the role of adult radioiodine exposure in the etiology of thyroid cancer remains to be clarified. The role of adult external radiation exposure is equally unclear.

Modifying factors. A radiation-associated increase in thyroid cancer incidence has been shown for both women and men, with women often having a somewhat higher excess relative risk (45, 48). It is of note, however, that in Belarus, there is little evidence of women having a greater susceptibility than men (39). This difference may be partly due to the very early age at diagnosis for many of the thyroid cancers, that is, at ages when there is little difference in the sex ratio of spontaneous thyroid cancers.

It has been suggested that radiation exposure in the presence of iodine deficiency might make people more susceptible to developing benign thyroid diseases and thyroid cancer (54, 60). This susceptibility may occur because the iodine deficiency results in greater radioiodine uptake and therefore dose, as well as hypothyroidism and increased thyroid-stimulating hormone. Elevated levels of thyroid-stimulating hormone are related to thyroid growth and possibly thyroid cancer (61, 62). In the Bryansk region of Russia, a twofold risk of childhood thyroid cancer was observed in highly deficient areas compared with regions that had normal iodine levels (63).

From the few studies that have reported quantified risks associated with Chernobyl exposure, the shape of the dose-response curve, the magnitude of the risks, and the patterns of modifying effects are consistent with those demonstrated for external radiation exposure. The excess absolute risks estimated from ecologic studies (42, 51) were about 50 percent lower than in the pooled analysis of childhood exposure to external radiation (25), but the differences were not significant. In contrast, the excess relative risk was about 2.5 times higher than that reported for the pooled analysis, but again it was not significantly different (42). From these risk estimates, the authors concluded that the carcinogenic effectiveness of ^{131}I relative to external X- or gamma radiation was less than unity based on an absolute risk model but above unity based on a relative risk model.

Clinical and molecular features. Both the clinical and molecular features of the thyroid cancers that developed following Chernobyl are unique. As expected for radiogenic thyroid cancers, the great majority of the cancers that occurred in children or young adults were papillary carcinomas; however, many had an unusual subtype that has a large solid component. The thyroid cancers also appeared to grow

rapidly and had high rates of local and distant metastasis (64–67). Although many of the cancers were aggressive, survival has been excellent. In Belarus, the survival rate was 99 percent for patients diagnosed between 1986 and 2002, with eight (0.7 percent) patients dying from the thyroid cancer (34). It is unclear whether the clinical presentation and course of the Chernobyl-related cancers is unusual or whether some of the findings represent a more general picture of thyroid carcinoma at young ages, or possibly when it occurs in conjunction with iodine deficiency, or very shortly after radiation exposure (2, 67, 68).

The frequency of *RET/PTC* rearrangements is high in post-Chernobyl childhood papillary thyroid cancers (69–71). The *PTC3* type is particularly common and has been associated with the solid variant of papillary cancer. Whether the *PTC3* rearrangements are due to radiation exposure or to the young age of the patients or early latency has not yet been established (67, 72). In a study of 67 Ukrainian patients, the frequency of rearrangements was about the same for young thyroid cancer patients whether they were exposed to Chernobyl or were born after the accident (72). Point mutations in the *BRAF* gene also have been found in papillary cancers (73, 74); however, unlike *RET* rearrangements, they occur most frequently in adult papillary carcinoma and are infrequent in childhood thyroid cancers (72, 75, 76). To date, no radiation “footprint” has been identified, and what once appeared to be radiation-related mutations may actually be age related.

Summary. Although there is still an excess of thyroid cancers in the territories near Chernobyl, the long-term time trends are not yet known. Of particular interest is whether the very rapid increase in incidence seen 5–10 years after the accident will continue. When an excess absolute risk model was used, there was no evidence of a downturn in risk between 1989 and 1998 (56). Learning more about time since exposure is important in trying to predict the future level of risk. Cardis et al. (55) predicted the lifetime number of thyroid cancers that would develop among children in Belarus less than age 5 years at the time of the accident. Depending on what statistical model was used, between 17,710 and 66,198 cases were estimated. The number of cases predicted is considerably larger than the approximately 12,000 predicted by Jacob et al. (51) to occur between 1997 and 2036.

In most assessments, both internal and external exposures appeared to be especially carcinogenic to the very young thyroid, and neither type of radiation has been clearly linked to adult exposure. As observed for external radiation, females generally have higher risks than males, but the differences are not statistically significant. A particularly short latency period has been demonstrated in Chernobyl, but this finding may be due to the large number of exposed persons and the early detection resulting from screening rather than to a true biologic difference. Further follow-up is needed to learn whether risks persist over time.

Leukemia

Although thyroid cancer was a primary concern in the aftermath of the Chernobyl accident, attention has also been

paid to a potential increased risk of leukemia due to the exposure to external radiation. Several ecologic studies have examined this possibility by using comparisons by time period (pre/postaccident) or extent of contamination.

Leukemia among those exposed in utero. Although, as mentioned above, there is little evidence concerning thyroid cancer among those exposed to Chernobyl radiation in utero, a series of studies have been carried out to examine leukemia risk in this population, stimulated by an initial report from Greece, which received some fallout from the accident (table 1) (77). The Greek study compared rates for cohorts born during “exposed” and “unexposed” periods and found a 2.6-fold increase (95 percent confidence interval: 1.4, 5.1) in leukemia risk among those in utero at the time of the accident. Elevated rates were also reported for those born in regions of Greece with higher levels of radioactive fallout (<6 kBq/m², 6–10 kBq/m², >10 kBq/m²). However, the numbers of cases in each exposure category were small, and the results were not confirmed when a similar approach comparing areas with the same categories of contamination was applied to analyzing data from the German Childhood Cancer Registry (78).

In a study in Belarus (79), where levels of contamination are higher by a factor of 10 or more, the results were similar to those in the Greek study, but the trend was weaker. Nevertheless, the highest annual incidence rate was in 1987, the year after the accident, and although numbers are small and the results nonsignificant statistically, the largest rate ratio (1.51, 95 percent confidence interval: 0.63, 3.61) was found in the two most contaminated regions of Belarus (Gomel and Mogilev).

A small study published by Noshchenko et al. (80) compares leukemia incidence during 1986–1996 among Ukrainian children born in 1986 and thus exposed in utero in the contaminated oblast of Zhitomir with children born in Poltava, a supposedly uncontaminated oblast. The reported risk ratios based on cumulative incidence show significant increases for all leukemia (rate ratio = 2.7, 95 percent confidence interval: 1.9, 3.8) and for acute lymphoblastic leukemia (rate ratio = 3.4, 95 percent confidence interval: 1.1, 10.4). The number of total cases was relatively small, however (21 in Zhitomir, eight in Poltava).

Leukemia among those exposed in childhood. Three registry-based studies (81–83) focused on possible risk among children in Belarus. None of the three studies, each with a different length of follow-up, reported excess rates of acute or other types of childhood leukemias in the post-accident period, either overall or in the most severely contaminated regions.

To our knowledge, only one analytic study of childhood leukemia (84) has been reported. The case-control study was based in two contaminated oblasts in Ukraine. Cases, diagnosed between 1987 and 1997, were under age 20 years at the time of the accident. Controls were randomly selected from the same oblast as the case and were matched on age at exposure, gender, and type of settlement (urban, rural). Although significant results are reported for subgroups in two time periods—acute leukemias among males who received doses of more than 10 mGy and were diagnosed between 1993 and 1997 and acute myeloid leukemia in the

period 1987–1992—the analysis was restricted to a small subset of the total cases, with no description of how they were selected.

One of the largest studies to date is the European Childhood Leukemia-Lymphoma Incidence Study (ECLIS), which examined rates of childhood leukemia in Belarus, Russia, and 33 other regions of Europe in relation to an estimated region- or country-specific exposure to Chernobyl fallout (85). Estimated doses had been calculated by the United Nations Scientific Committee on the Effects of Atomic Radiation (3) using models based on direct measurements carried out in the year after the accident (86). Rates of childhood leukemia were higher in the postaccident period, but there was no trend with radiation dose. However, the study design treating both dose and cancer rates at the regional or national level had only limited power to detect a small effect if there were one, given the misclassification inherent in such a metric.

Leukemia among those exposed as adults. Only a few studies have been conducted examining leukemia incidence in adult residents of exposed areas. Age-specific leukemia incidence rates in three contaminated regions of Ukraine (87) were examined by year of diagnosis, before and after the accident (through 1990). Increases were seen only in the age group 65 years or older, suggesting heightened medical surveillance rather than an effect of exposure.

Time trends were also examined in the Kaluga oblast of the Russian Federation 10 years postaccident (47). Rate ratios were similar before and after the accident or steadily increased with time, and no increase in leukemia occurred in the most contaminated areas of the oblast. In Ukraine (88), incidence rates increased postaccident from 5.1 per 100,000 to 11.0 per 100,000, but rates were not higher in the more contaminated areas.

Summary. To date, the available evidence does not indicate an effect of Chernobyl fallout on leukemia risk among residents of contaminated areas exposed either as children or as adults. The great majority of studies have relied on available data from registries. Although ecologic studies do not have much power to detect small effects, if increases were occurring of the same magnitude as those for thyroid cancer in children, they would likely have been picked up by now.

There is a suggestion that leukemia risk may be raised for persons exposed in utero. The hypothesis that low-dose fetal irradiation may damage hematopoietic processes may merit further consideration but primarily on the basis of biologic assumptions about susceptibility and evidence from external radiation rather than the results of studies of Chernobyl fallout, which are conflicting.

Other cancers

Scant evidence exists concerning risk of solid tumors, other than thyroid cancer, among residents of contaminated areas. What evidence there is is difficult to interpret since follow-up periods are generally shorter than the latency periods for these cancers, and the ecologic study designs used to date have not generally permitted adjustment for potential confounding variables.

One of the series of reports by Ivanov et al. (47) analyzed time trends and relative population risks among adults in a contaminated oblast in the Russian Federation. Data came from a computerized cancer registry, part of the Russian National Medical and Dosimetric Registry, and included approximately 10 years of follow-up postaccident. Average ^{137}Cs contamination densities were based on models of the composition of the fallout and atmospheric transport. Standardized incidence and mortality ratios were similar before and after the Chernobyl accident. Ratios for cancers of the respiratory organs among women from the contaminated areas were raised, but the increase was not significant.

Breast cancer is of interest because of its sensitivity to external radiation and because lactating women receive higher doses of radioiodines. We know of no descriptive or analytic studies concerning breast cancer risk in exposed populations that have been published in peer-reviewed journals. However, a monograph report (89) has shown an increase in premenopausal breast cancer in women from contaminated areas of Ukraine close to Chernobyl compared with Ukraine female population rates (standardized incidence ratio = 1.50, 95 percent confidence interval: 1.27, 1.73).

As the length of time since the accident increases to almost 20 years, there is interest in pursuing the lead with respect to breast cancer as well as in examining patterns with other solid tumors.

Other outcomes

Consideration of noncancer endpoints is beyond the scope of this review. However, research is being conducted in a number of different areas, including nonmalignant thyroid disease, cardiovascular disease, cataracts, adverse pregnancy outcomes, psychological and cognitive status of children, and mental health and well-being of the population. A World Health Organization report of the Chernobyl Forum's Expert Group Health summarizes this work (34).

CONCLUSION

Because of the magnitude and extent of the radioactive releases and the size of the exposed population, the Chernobyl accident is a man-made, nuclear disaster of unparalleled proportions. From the Chernobyl disaster, however, we have learned a great deal about childhood exposure to ^{131}I . In general, there appears to be much in common between the role of external and internal radiation in the development of thyroid cancer. Given all of the uncertainties in dose estimates, the role of screening in case ascertainment, and the small numbers for some of the observations, the magnitude of the excess risks is consistent. Following either internal or external radiation, the thyroid of young children is more vulnerable to radiation carcinogenesis than that of adults, radiation-related risks may be somewhat higher for females than males, and excess risks are still observed 18 years after the accident. Gaps still need to be filled, however. Of particular interest is whether some of the findings to date are related to Chernobyl specifically or to the characteristics of thyroid cancer in very young

TABLE 5. Summary of findings* to date on Chernobyl fallout and cancer risk following the 1986 nuclear power plant accident

Exposed population	Thyroid cancer	Leukemia	Other cancers
Cleanup workers	?	+	0
Residents of contaminated areas			
Children	+ + +	—	0
In utero	0	+ ?	0
Adults	—	—	—

* +, positive; —, no association; 0, data lacking; ?, equivocal.

children or the very short latency period between radiation exposure and the development of thyroid cancer. Little is known about the potential modifying effects of prior thyroid disease, hormonal and reproductive factors, diet, or ethnic differences. Finally, because the Chernobyl-related thyroid cancers are known to be caused by radiation, these cancers are a unique resource for studying the molecular biology of radiation- and non-radiation-induced thyroid cancer. This field is continuing to advance and should increase our understanding of thyroid cancer in general.

With respect to adults, it appears that although risks of thyroid cancer and leukemia are not elevated among residents of contaminated areas, increases in leukemia are being observed in those exposed to external radiation during cleanup operations. There is also a suggestion of heightened risk among those exposed in utero. (Refer to table 5 for a summary.)

Although we have not covered the topic of disaster preparedness in this review, the Chernobyl accident has provided valuable experience in this area, particularly with regard to the administration of potassium iodide as a preventive measure. Furthermore, the accidental exposure of children to radioiodines has generated information that will be relevant in evaluating the use of ^{131}I in treating children with hyperthyroidism. The opportunity to compare outcomes in different population subgroups, such as workers or residents exposed as children or as adults, contributes to our understanding of dose-response relations and moderating factors and, in the case of cleanup workers, should provide input for formulating guidelines to protect the health of nuclear workers.

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